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DATE: Thursday, November 10, 2005

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END OF SEARCH HISTORY

DIALOG(R)File 654:US Pat.Full.

4753431
Derwent Accession: 1999-580417
Utility
C/ Methods for using %heat% %shock% %proteins%
Inventor: Wallen, Erik, Albuquerque, NM
Moseley, Pope L., Albuquerque, NM
Assignee: University of New Mexico (02), Albuquerque, NM
New Mexico, University of (Code: 14014)
Examiner: Jones, Dwayne C. (Art Unit: 164)
Assistant Examiner: Delacroix-Muirhei, C.
Law Firm: Jagtiani + Guttag

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6455493	A	20020924	US 99276468	19990325
CIP	US 5981706	A		US 97986234	19971205
CIP	US 6066716	A		US 97934139	19970919
CIP	US 5747332	A		US 96717239	19960920

Fulltext Word Count: 3631

Abstract:
The present invention provides a %heat% %shock% %protein% immunotoxin comprising: at least a fragment of a %heat% %shock% %protein%, the fragment being capable of being bound by an immune cell; and a toxin bound to the fragment. The present invention also provides a method for decreasing the number of immune cells in an individual using the %heat% %shock% %protein% immunotoxins of the present invention. In addition, the present invention provides a method for decreasing the number of immune cells in an organ using the %heat% %shock% %protein% immunotoxins of the present invention.

5/3,AB/53 (Item 35 from file: 654)
DIALOG(R)File 654:US Pat.Full.

4748665
Derwent Accession: 2000-317604
Utility
CERTIFICATE OF CORRECTION
C/ Methods for generating antigen-reactive T cells in vitro
; INCUBATING T-CELLS AND ANTIGEN PRESENTING CELLS IN VITRO WITH PURIFIED COMPLEX OF %HEAT% %SHOCK% %PROTEIN% AND ANTIGEN; GENERATING CD4 CELLS; IMMUNOTHERAPY, ANTICARCINOGENIC AGENTS
Inventor: Srivastava, Pramod K., Avon, CT
Assignee: University of Conneticut Health Center (02), Farmington, CT
Connecticut, University of (Code: 02814)
Examiner: Bansal, Geetha P. (Art Unit: 162)
Law Firm: Pennie & Edmonds LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6451316	A	20020917	US 98166401	19981005

Fulltext Word Count: 20359

Abstract:
The present invention provides methods for generating antigen-reactive T cells in vitro comprising priming immune cells and incubating the primed immune cells in vitro with a non-covalent complex of an %heat% %shock% %protein% and an antigenic molecule. The present invention further relates to methods for generating antigen-reactive CD4+ T cells

; %BIND%%ING H%%EAT SHO%%CK P%%ROTEI%%N TO DE%NATURED PROTEIN MATRIX, ADDING COMPLEXING SOLUTION CONTAINING A PEPTIDE TO ELUTE A %HEAT% %SHOCK% %PROTEIN%-PEPTIDE %COMPLEX%; PRODUCTION OF ANTICARCINOGENIC/ANTITUMOR PEPTIDE-BASED VACCINES
Inventor: Wallen, Erik S., Albuquerque, NM
Moseley, Pope L., Albuquerque, NM
Assignee: University of New Mexico (02), Albuquerque, NM
New Mexico, University of (Code: 14014)
Examiner: Tsang, Cecilia J. (Art Unit: 164)
Assistant Examiner: Delacroix-Muirheid, C.
Law Firm: Jagtianai & Associate

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 5981706	A	19991109	US 97986234	19971205
CIP	US 5747332	A		US 96717239	19960920
	Pending			US 97934139	19970919

Fulltext Word Count: 3452

Abstract:
The present invention provides a method for synthesizing %heat% %shock% %protein%-peptide complexes comprising the steps of: adding a shock protein to a denatured protein matrix to bind the %heat% %shock% %protein% to the denatured protein matrix; and adding a complexing solution comprising a peptide to elute a %heat% %shock% %protein%-peptide %complex%. The present invention also provides a %heat% %shock% %protein%-peptide %complex% synthesized by the method of the invention. In addition the present invention provides an apparatus for synthesizing %heat% %shock% %protein%-peptide complexes comprising a %heat% %shock% %protein% %complex% bound to a denatured protein matrix.

5/3,AB/58 (Item 40 from file: 654)
DIALOG(R)File 654:US Pat.Full.

4209023
Derwent Accession: 1995-336815
Utility
REASSIGNED
C/ Stress protein-peptide complexes as prophylactic and therapeutic vaccines against intracellular pathogens
; COMPLEX OF A MAMMALIAN STRESS PROTEIN NONCOVALENTLY ASSOCIATED WITH A PEPTIDE THAT IS PRESENT IN A EUKARYOTIC CELL INFECTED WITH SAID PATHOGEN BUT NOT PRESENT IN SAID CELL WHEN SAID CELL IS NOT INFECTED WITH SAID PATHOGEN
Inventor: Srivastava, Pramod K., Riverdale, NY
Assignee: Mount Sinai School of Medicine of the City University of New York (02), New York, NY
Mount Sinai School of Medicine of City Univ of New York (Code: 57466)
Examiner: Hutzell, Paula K. (Art Unit: 162)
Assistant Examiner: Bansal, Geetha P.
Law Firm: Pennie & Edmonds LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 5961979	A	19991005	US 94210421	19940316

Fulltext Word Count: 19940

Abstract:
Disclosed is a family of vaccines that contain stress protein-peptide complexes which when administered to a mammal are operative at initiating

present invention, the reference and test fingerprints are based on cellular assays (but not on assays of whole multicellular organisms, or their organs or tissues).

French Abstract
La presente invention permet de prevoir l'aptitude d'un compose d'interet a moduler l'activite biologique d'un recepteur dans un organisme multicellulaire a partir de son interaction avec ledit recepteur en presence de divers membres d'un groupe de bio-cles. Les bio-cles sont des ligands, en particulier des peptides ou des acides nucleiques, connus pour modifier la conformation du recepteur. Ces donnees d'interaction constituent ce que l'on appelle une "empreinte digitale", qui est comparee aux empreintes de composes de reference aux activites biologiques connues et dont le recepteur assure la mediation. Dans la realisation dite "en braille moleculaire" de la presente invention, les empreintes digitales de reference et de test sont basees sur des essais i(in vitro) (acellulaires). Dans la realisation dite "en braille cellulaire" de la presente invention, les empreintes digitales de reference et de test sont basees sur des essais cellulaires (mais non pas sur des essais d'organismes multicellulaires complets, ou de leurs organes ou tissus).

7/3,AB/62 (Item 19 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00497830
METHOD FOR PURIFYING HEAT SHOCK PEPTIDES COMPLEXES
PROCEDE SERVANT A PURIFIER DES COMPLEXES DE PEPTIDES ET DE PROTEINES DU STRESS
Patent Applicant/Assignee:
THE UNIVERSITY OF NEW MEXICO,
Inventor(s):
WALLEN Erik S,
MOSELEY Pope L,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9929182 A1 19990617
Application: WO 98US25734 19981204 (PCT/WO US9825734)
Priority Application: US 97985548 19971205; US 97986234 19971205
Designated States: BR CA JP MX AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 5670

English Abstract
The present invention provides a method for synthesizing %heat% %shock% %protein%-peptide complexes comprising the steps of: adding a shock protein to a denatured protein matrix to bind the %heat% %shock% %protein% to the denatured protein matrix; and adding a complexing solution comprising a peptide to elute a %heat% %shock% %protein%-peptide %complex%. The present invention also provides a %heat% %shock% %protein% -peptide %complex% synthesized by the method of the invention. In addition the present invention provides an apparatus for synthesizing %heat% %shock% %protein%-peptide complexes comprising a %heat% %shock% %protein% %complex% bound to a denatured protein matrix. The present invention also provides a method for treating an allergic disease in which a %heat% %shock% %protein%-antigen %complex% is administered to a mammal in an amount sufficient to reduce the susceptibility of the mammal to a Th2 response for the allergic disease. The method of the present invention can be used either to prevent an invididual from having an allergic reaction to an allergic disease or to reduce the effects of an allergic disease in an individual already suffering from the allergic disease.

French Abstract
L'invention concerne un procede servant a realiser la synthese de complexes constitues par des peptides et par des proteines du stress et consistant a effectuer l'apport d'une proteine du stress a une matrice de

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Search Results - Record(s) 1 through 25 of 25 returned.

☐ 1. Document ID: US 20050221421 A1

Using default format because multiple data bases are involved.

L1: Entry 1 of 25 File: PGPB Oct 6, 2005

PGPUB-DOCUMENT-NUMBER: 20050221421
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050221421 A1

TITLE: Method of producing and using heat shock proteins

PUBLICATION-DATE: October 6, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Tran, Jean-Luc V.	Camden	NJ	US
Hewitt, Charles W.	Blackwood	NJ	US

US-CL-CURRENT: 435/69.1; 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 20050221395 A1

L1: Entry 2 of 25 File: PGPB Oct 6, 2005

DOCUMENT-IDENTIFIER: US 20050221395 A1
TITLE: Methods and products based on oligomerization of stress proteins

Detail Description Paragraph:
[0336] APCs can be sensitized with hsp bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7/ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 3. Document ID: US 20040253228 A1

L1: Entry 3 of 25 File: PGPB Dec 16, 2004

DOCUMENT-IDENTIFIER: US 20040253228 A1
TITLE: Methods for using compositions comprising heat shock proteins or alpha-2-macroglobulin in the treatment of cancer and infectious disease

Detail Description Paragraph:
[0252] APC are sensitized with HSP or .alpha.2M bound to antigenic peptides preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of HSPs or .alpha.2M and antigenic molecules by incubating in vitro with the HSP-complex or .alpha.2M-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 dendritic cells can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram HSP90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7/ml) for injection in a patient. Preferably, the patient into which the sensitized dendritic cells are injected is the patient from which the dendritic cells were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 4. Document ID: US 20030129196 A1

L1: Entry 4 of 25 File: PGPB Jul 10, 2003

DOCUMENT-IDENTIFIER: US 20030129196 A1
TITLE: Methods for preparing compositions comprising heat shock proteins or alpha-2-macroglobulin useful for the treatment of cancer and infectious disease

Summary of Invention Paragraph:
[0188] APC are sensitized with HSP or .alpha.2M bound to antigenic peptides preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of HSPs or .alpha.2M and antigenic molecules by incubating in vitro with the HSP-complex or .alpha.2M-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 dendritic cells can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram HSP90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7/ml) for injection in a patient. Preferably, the patient into which the sensitized dendritic cells are injected is the patient from which the dendritic cells were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 5. Document ID: US 20030012794 A1

L1: Entry 5 of 25 File: PGPB Jan 16, 2003

DOCUMENT-IDENTIFIER: US 20030012794 A1
TITLE: Kits comprising heat shock protein-antigenic molecule complexes

Detail Description Paragraph:
[0125] APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7/ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D...

☐ 6. Document ID: US 20020172682 A1

L1: Entry 6 of 25 File: PGPB Nov 21, 2002

DOCUMENT-IDENTIFIER: US 20020172682 A1
TITLE: Using heat shock proteins to increase immune response

Detail Description Paragraph:
[0215] APC can be activated with an HSP or .alpha.2M preparation of the invention by incubating the cells in vitro with the complexes. Preferably, the APC are activated with a HSP preparation or .alpha.2M preparation by incubating in vitro with the hsp-complex or .alpha.2M-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96 per ml or 100 microgram hsp90 per ml at 37.degree. C. for 15 minutes to 24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7/ml) for infusion in a patient. Preferably, the patient into which the sensitized APCs are infused is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D...

☐ 7. Document ID: US 6455048 B1

L1: Entry 7 of 25 File: USPT Sep 24, 2002

DOCUMENT-IDENTIFIER: US 6455048 B1
TITLE: Prevention of primary and metastatic neoplastic diseases with hsp70-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 8. Document ID: US 6447780 B1

L1: Entry 8 of 25 File: USPT Sep 10, 2002

DOCUMENT-IDENTIFIER: US 6447780 B1
TITLE: Prevention of primary and metastatic neoplastic diseases with hsp90-peptide complexes

Detailed Description Text (102):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4-10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 9. Document ID: US 6436404 B1

L1: Entry 9 of 25 File: USPT Aug 20, 2002

DOCUMENT-IDENTIFIER: US 6436404 B1
TITLE: Prevention of primary and metastatic neoplastic diseases with GP96-peptide

complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 10. Document ID: US 6403095 B1

L1: Entry 10 of 25 File: USPT Jun 11, 2002

DOCUMENT-IDENTIFIER: US 6403095 B1
TITLE: Treatment of primary and metastatic neoplastic diseases with HSP70-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 11. Document ID: US 6399070 B1

L1: Entry 11 of 25 File: USPT Jun 4, 2002

DOCUMENT-IDENTIFIER: US 6399070 B1
TITLE: Methods and compositions for eliciting an immune response with hsp90-peptide complexes

Detailed Description Text (104):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 12. Document ID: US 6399069 B1

L1: Entry 12 of 25 File: USPT Jun 4, 2002

DOCUMENT-IDENTIFIER: US 6399069 B1
TITLE: Prevention of infectious diseases with hsp70-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 13. Document ID: US 6391306 B1

L1: Entry 13 of 25 File: USPT May 21, 2002

DOCUMENT-IDENTIFIER: US 6391306 B1
TITLE: Treatment of infectious diseases with hsp90-peptide complexes

Detailed Description Text (103):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not

limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment)

☐ 14. Document ID: US 6387374 B1

L1: Entry 14 of 25 File: USPT May 14, 2002

DOCUMENT-IDENTIFIER: US 6387374 B1
TITLE: Treatment of primary and metastatic neoplastic diseases with hsp90-peptide complexes

Detailed Description Text (104):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 15. Document ID: US 6383494 B1

L1: Entry 15 of 25 File: USPT May 7, 2002

DOCUMENT-IDENTIFIER: US 6383494 B1
TITLE: Methods and composition for eliciting an immune response with gp96-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are

washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 16. Document ID: US 6383493 B1

L1: Entry 16 of 25 File: USPT May 7, 2002

DOCUMENT-IDENTIFIER: US 6383493 B1
TITLE: Methods and compositions for eliciting an immune response with hsp70-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

☐ 17. Document ID: US 6383492 B1

L1: Entry 17 of 25 File: USPT May 7, 2002

DOCUMENT-IDENTIFIER: US 6383492 B1
TITLE: Treatment of infectious diseases with gp96-peptide complexes

Brief Summary Text (152):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (aueologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 18. Document ID: US 6383491 B1

L1: Entry 18 of 25 File: USPT May 7, 2002

DOCUMENT-IDENTIFIER: US 6383491 B1
TITLE: Prevention of infectious diseases with hsp90-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antotigenic molecules preferably by incubating the cells in vitro with the complexes. The APd are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 19. Document ID: US 6379672 B1

L1: Entry 19 of 25 File: USPT Apr 30, 2002

DOCUMENT-IDENTIFIER: US 6379672 B1
TITLE: Prevention of infectious diseases with gp96-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times. and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 20. Document ID: US 6375953 B1

L1: Entry 20 of 25 File: USPT Apr 23, 2002

DOCUMENT-IDENTIFIER: US 6375953 B1
TITLE: Treatment of infectious diseases with HSP70-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 21. Document ID: US 6322790 B1

L1: Entry 21 of 25 File: USPT Nov 27, 2001

DOCUMENT-IDENTIFIER: US 6322790 B1
TITLE: Compositions and methods for eliciting an immune response using heat shock/stress protein-peptide complexes in combination with adoptive immunotherapy

Brief Summary Text (190):
APC are sensitized with hap noncovalantly bound to antigenic molecules by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules preferably by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 22. Document ID: US 6156302 A

L1: Entry 22 of 25 File: USPT Dec 5, 2000

DOCUMENT-IDENTIFIER: US 6156302 A
TITLE: Adoptive immunotherapy using macrophages sensitized with heat shock protein-epitope complexes

Detailed Description Text (87):
APC are sensitized with hsp noncovalently bound to antigenic molecules by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 min.-24 hrs. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90 -peptide complexes per ml at 37.degree. C. for 15 min.-24 hrs. in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for infusion in a patient. Preferably, the patient into which the sensitized APCs are infused is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 23. Document ID: US 6017540 A

L1: Entry 23 of 25 File: USPT Jan 25, 2000

DOCUMENT-IDENTIFIER: US 6017540 A
TITLE: Prevention and treatment of primary and metastatic neoplastic diseases and infectious diseases with heat shock/stress protein-peptide complexes

Detailed Description Text (105):
APC are sensitized with hsp noncovalently bound to antigenic molecules preferably by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 24. Document ID: US 5985270 A

L1: Entry 24 of 25 File: USPT Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5985270 A
TITLE: Adoptive immunotherapy using macrophages sensitized with heat shock protein-

epitope complexes

Detailed Description Text (87):
APC are sensitized with hsp non-covalently bound to antigenic molecules by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules by incubating in vitro with the hsp-complex at 37.degree. C. for 15 min.-24 hrs. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 min.-24 hrs. in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for infusion in a patient. Preferably, the patient into which the sensitized APCs are infused is the patient from which the APC were originally isolated (autologous embodiment).

☐ 25. Document ID: US 5830464 A

L1: Entry 25 of 25 File: USPT Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830464 A
** See image for Certificate of Correction **
TITLE: Compositions and methods for the treatment and growth inhibition of cancer using heat shock/stress protein-peptide complexes in combination with adoptive immunotherapy

Brief Summary Text (145):
APC are sensitized with hsp noncovalently bound to antigenic molecules by incubating the cells in vitro with the complexes. The APC are sensitized with complexes of hsps and antigenic molecules preferably by incubating in vitro with the hsp-complex at 37.degree. C. for 15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed three times and resuspended in a physiological medium preferably sterile, at a convenient concentration (e.g., 1.times.10.sup.7 /ml) for injection in a patient. Preferably, the patient into which the sensitized APCs are injected is the patient from which the APC were originally isolated (autologous embodiment).

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Term	Documents
CPNCOMPLEXES	0
CPNCOMPLEX	0

CPN-COMPLEXS	0
CPN-COMPLEX	0
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HSP-COMPLEXS	0
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STPCOMPLEX	0
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STP-COMPLES	0
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☐	L2	(Groel near groes) same immun$	22

END OF SEARCH HISTORY

Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Brucella abortus resists the microbicidal mechanisms of macrophages, and the expression of its heat shock proteins (HSPs) such as GroEL, **GroES** and HtrA may play a role in this resistance. Bacterial HSPs can be very immunogenic, inducing protective immunity in various types of bacterial infections. However, the significance of immune responses directed against B. abortus HSPs in the protection against brucellosis is currently unresolved. To elucidate the role of these proteins in protection against Brucella challenge, individual, divalent or trivalent baculovirus (BV) recombinants of B. abortus GroEL, **GroES** and/or HtrA were injected into BALB/c mice either as protein-expressing whole cells or as purified proteins. The preparations were given to mice in combination with Freund's or Ribi adjuvant, respectively. In addition, some mice were primed with a **vaccinia** virus-GroEL recombinant, followed by inoculation with purified GroEL-Ribi adjuvant combination. Antibodies were observed against B. abortus GroEL and HtrA, but not against **GroES** . Cellular immune response was demonstrated by observing significant IFN-gamma release by lymphocytes of mice immunized with the purified HtrA-Ribi adjuvant combination. However, none of the mice inoculated with individual, divalent or trivalent HSP-expressing cells combined with complete Freund's adjuvant or inoculated with purified B. abortus HSPs combined with Ribi adjuvant, were protected against challenge with B. abortus virulent strain 2308. Priming with **vaccinia** virus-GroEL recombinant and boosting with GroEL-Ribi combination did not induce protective immunity. Based on the results obtained, we suggest that although humoral and cell-mediated immune responses are induced, but protective immune response is not induced by B. abortus HSPs.

Tags: Female; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Antibodies, Bacterial--biosynthesis--BI; *Bacterial **Vaccines** --immunology--IM; *Brucella abortus--immunology--IM; *Heat-Shock Proteins--immunology--IM; Animals; Baculoviridae; Brucellosis--prevention and control--PC; **GroEL Protein** --immunology--IM; **GroES** Protein --immunology--IM; Immunity, Cellular; Mice; Mice, Inbred BALB C; Periplasmic Proteins--immunology--IM; Serine Endopeptidases--immunology--IM ; **Vaccination** ; **Vaccines, Synthetic** --immunology--IM; **Vaccinia** virus

CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Bacterial Vaccines); 0 (GroEL Protein); 0 (GroES Protein); 0 (Heat-Shock Proteins); 0 (Periplasmic Proteins); 0 (Vaccines, Synthetic)

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (DegP protease)

Record Date Created: 20020723
Record Date Completed: 20021126

19/9/4
DIALOG(R)File 155:MEDLINE(R)

12941453 PMID: 10889410

Cloning and kinetics of expression of Brucella abortus heat shock proteins by baculovirus recombinants.

Bae J E; Toth T E

Department of Biomedical Sciences and Pathobiology, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061-0342, USA.

Veterinary microbiology (NETHERLANDS) Jul 31 2000, 75 (2) p199-204, ISSN 0378-1135 Journal Code: 7705469

Publishing Model Print

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

In an effort to develop genetically engineered Brucella abortus (BA) **vaccines** , the genes encoding heat shock proteins (HSPs) GroEL, **GroES** , and HtrA were cloned and expressed in the BAC-TO-BAC Baculovirus System, and the kinetics of protein expression were analyzed using various insect cell lines in suspension cultures, different cell densities in suspension cultures, multiplicities of infection and recombinant virus replication times. Trichoplusia ni cells expressed only BA HtrA, but Spodoptera frugiperda (Sf9) cells expressed all three recombinant proteins. The best GroEL expression was achieved by infecting 2x10(6) Sf9 cells/ml with an MOI 10 of recombinant virus and harvesting the cells after 96h of virus replication. **GroES** and HtrA were best expressed when infecting 2x10(6) Sf9 cells/ml with an MOI 1 of recombinant viruses and harvesting the cells after 120h of virus replications. Under these conditions BA recombinant HSPs were expressed as follows: GroEL at 16% of the total cellular proteins (105microg/ml concentration); **GroES** 2% (15.25microg/ml); and HtrA 8% (84.48microg/ml). This is the first report of cloning and expression of BA genes in the baculovirus system.

Tags: Female; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Brucella abortus--immunology--IM; *Brucellosis, Bovine --immunology--IM; *Heat-Shock Proteins--immunology--IM; *Periplasmic Proteins; Animals; Antibodies, Monoclonal; Bacterial Proteins--chemistry --CH; Bacterial Proteins--genetics--GE; Bacterial Proteins--immunology --IM; Bacterial **Vaccines** --immunology--IM; Blotting, Southern--veterinary --VE; Blotting, Western--veterinary--VE; Brucella abortus--genetics--GE; Brucellosis, Bovine--prevention and control--PC; Cattle; Cell Line; Cloning, Molecular; Electrophoresis, Polyacrylamide Gel--veterinary--VE; **GroEL Protein** --chemistry--CH; **GroEL Protein** --genetics--GE; **GroEL Protein** --immunology--IM; **GroES** Protein--chemistry--CH; **GroES** Protein --genetics--GE; **GroES** Protein--immunology--IM; Heat-Shock Proteins --chemistry--CH; Heat-Shock Proteins--genetics--GE; Recombinant Fusion Proteins--chemistry--CH; Serine Endopeptidases--chemistry--CH; Serine Endopeptidases--genetics--GE; Serine Endopeptidases--immunology--IM; Spodoptera

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Bacterial Proteins); 0 (Bacterial Vaccines); 0 (GroEL Protein); 0 (GroES Protein); 0 (Heat-Shock Proteins); 0 (Periplasmic Proteins); 0 (Recombinant Fusion Proteins)

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (DegP protease)

Record Date Created: 20000831
Record Date Completed: 20000831

19/9/5

09777734 PMID: 1350274

Characterization of the heat shock response in Brucella abortus and isolation of the genes encoding the GroE heat shock proteins.

Lin J; Adams L G; Ficht T A

Department of Veterinary Pathobiology, Texas A&M University, College Station 77843-4467.

Infection and immunity (UNITED STATES) Jun 1992, 60 (6) p2425-31, ISSN 0019-9567 Journal Code: 0246127

Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

In an effort to define the heat shock response in the bovine intracellular pathogen Brucella abortus, a rough variant lacking extensive lipopolysaccharide was pulse-labeled with [35S]methionine following exposure to elevated temperatures. The major heat shock proteins observed following sodium dodecyl sulfate-polyacrylamide gel electrophoresis and autoradiography migrate at 70, 62, 18, and 10 kDa. The maximum response was observed between 42 and 46 degrees C and within 2 to 3 h of the shif in temperature and varied slightly for the different proteins. Accumulation of the 62-kDa heat shock protein (62-kDa Hsp) was observed to continue for up to 5 h following the shift in temperature. In an effort to better define the heat shock response and its potential relationship with protective immunity, genes encoding the major heat shock proteins were isolated from recombinant libraries constructed from B. abortus S19 and S2308 and sequenced. The 62-kDa Hsp shares more than 60% amino acid homology with members of the GroEL family and is immunoprecipitated with polyclonal antibodies to Escherichia coli GroEL and monoclonal antibodies to mycobacterial Hsp 65. Western blot (immunoblot) analysis with pooled sera from **vaccinated** and infected cattle revealed that the 62-kDa Hsp is a predominantly recognized antigen. The roles of these gene products during environmental stress and in protective immunity against brucellosis are under investigation.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Bacterial Proteins--genetics--GE; *Brucella abortus --genetics--GE; *Genes, Bacterial; *Heat; *Heat-Shock Proteins--genetics --GE; Amino Acid Sequence; Animals; Bacterial Proteins--analysis--AN; Bacterial Proteins--immunology--IM; Base Sequence; Brucellosis, Bovine --metabolism--ME; Cattle; **GroEL Protein** ; **GroES** Protein; Heat-Shock Proteins--analysis--AN; Heat-Shock Proteins--immunology--IM; Molecular Sequence Data; Rabbits; **Vaccination**

Molecular Sequence Databank No.: GENBANK/M63610; GENBANK/M63611; GENBANK/M63612; GENBANK/M63613; GENBANK/M63614; GENBANK/M63615; GENBANK/M63616; GENBANK/M63617; GENBANK/M83930; GENBANK/X63185

CAS Registry No.: 0 (Bacterial Proteins); 0 (GroEL Protein); 0 (GroES Protein); 0 (Heat-Shock Proteins)

Record Date Created: 19920623
Record Date Completed: 19920623

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14442389 PMID: 12381581

Genetic immunization with Ehrlichia ruminantium GroEL and GroES homologues.

Pretorius Alri; Van Strijp F; Brayton K A; Collins N E; Allsopp B A

Molecular Biology Section, Onderstepoort Veterinary Institute, Pretoria, South Africa. Alri@moon.ovi.ac.za

Annals of the New York Academy of Sciences (United States) Oct 2002, 969 p151-4, ISSN 0077-8923 Journal Code: 7506858

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Ehrlichia ruminantium GroEL and **GroES** genes were amplified from E. ruminantium Welgevonden genomic DNA and were cloned into genetic **vaccine** and Salmonella expression vectors. These constructs were used to inoculate Balb/c and C57BL/6J mice. Both GroEL and **GroES** induced low levels of protection in Balb/c and C57BL/6J mice immunized with the Salmonella expression vectors. None of the mice inoculated with the genetic **vaccine** survived. Immunological memory was also tested in these mice and a correlation between splenocyte proliferation and the survival rate was observed.

Descriptors: *Bacterial **Vaccines** ; *Ehrlichia ruminantium--immunology --IM; * **GroEL Protein** --immunology--IM; * **GroES** Protein--immunology--IM; *Heartwater Disease--prevention and control--PC; Animals; Antigens, Bacterial--genetics--GE; Antigens, Bacterial--immunology--IM; Bacterial **Vaccines** --genetics--GE; Bacterial **Vaccines** --immunology--IM; DNA, Bacterial--immunology--IM; Ehrlichia ruminantium--genetics--GE; Gene Amplification; Genetic Vectors; **GroEL Protein** --genetics--GE; **GroES** Protein--genetics--GE; Immunization; Immunologic Memory; Lethal Dose 50; Lymphocyte Activation; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Salmonella; Spleen--cytology--CY; **Vaccines** , DNA; **Vaccines** , Synthetic --genetics--GE; **Vaccines** , Synthetic--immunology--IM

CAS Registry No.: 0 (Antigens, Bacterial); 0 (Bacterial Vaccines); 0 (DNA, Bacterial); 0 (Genetic Vectors); 0 (GroEL Protein); 0 (GroES Protein); 0 (Vaccines, DNA); 0 (Vaccines, Synthetic)

Record Date Created: 20021016

Record Date Completed: 20021211

19/9/3

14319527 PMID: 12135637

Mice immune responses to Brucella abortus heat shock proteins. Use of baculovirus recombinant-expressing whole insect cells, purified Brucella abortus recombinant proteins, and a vaccinia **virus recombinant as immunogens.**

Bae J E; Schurig G G; Toth T E

Department of Biomedical Sciences and Pathobiology, Center for Molecular Medicine and Infectious Diseases, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, 24061-0342, Blacksburg, VA, USA

Veterinary microbiology (Netherlands) Aug 25 2002, 88 (2) p189-202, ISSN 0378-1135 Journal Code: 7705469

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

14442389 PMID: 12381581

Genetic immunization with Ehrlichia ruminantium GroEL and GroES homologues.

Pretorius Alri; Van Strijp F; Brayton K A; Collins N E; Allsopp B A

Molecular Biology Section, Onderstepoort Veterinary Institute, Pretoria, South Africa. Alri@moon.ovi.ac.za

Annals of the New York Academy of Sciences (United States) Oct 2002, 969 p151-4, ISSN 0077-8923 Journal Code: 7506858

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Ehrlichia ruminantium GroEL and GroES genes were amplified from E. ruminantium Welgevonden genomic DNA and were cloned into genetic **vaccine** and Salmonella expression vectors. These constructs were used to inoculate Balb/c and C57BL/6J mice. Both GroEL and GroES induced low levels of protection in Balb/c and C57BL/6J mice immunized with the Salmonella expression vectors. None of the mice inoculated with the genetic **vaccine** survived. Immunological memory was also tested in these mice and a correlation between splenocyte proliferation and the survival rate was observed.

Descriptors: *Bacterial **Vaccines** ; *Ehrlichia ruminantium--immunology --IM; * **GroEL Protein** --immunology--IM; * **GroES** Protein--immunology--IM; *Heartwater Disease--prevention and control--PC; Animals; Antigens, Bacterial--genetics--GE; Antigens, Bacterial--immunology--IM; Bacterial **Vaccines** --genetics--GE; Bacterial **Vaccines** --immunology--IM; DNA, Bacterial--immunology--IM; Ehrlichia ruminantium--genetics--GE; Gene Amplification; Genetic Vectors; **GroEL Protein** --genetics--GE; **GroES** Protein--genetics--GE; Immunization; Immunologic Memory; Lethal Dose 50; Lymphocyte Activation; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Salmonella; Spleen--cytology--CY; **Vaccines** , DNA; **Vaccines** , Synthetic

--genetics--GE; **Vaccines** , Synthetic--immunology--IM

CAS Registry No.: 0 (Antigens, Bacterial); 0 (Bacterial Vaccines); 0 (DNA, Bacterial); 0 (Genetic Vectors); 0 (GroEL Protein); 0 (GroES Protein); 0 (Vaccines, DNA); 0 (Vaccines, Synthetic)

Record Date Created: 20021016

Record Date Completed: 20021211

14319527 PMID: 12135637

Mice immune responses to Brucella abortus heat shock proteins. Use of baculovirus recombinant-expressing whole insect cells, purified Brucella abortus recombinant proteins, and a vaccinia virus recombinant as immunogens.

Bae J E; Schurig G G; Toth T E

Department of Biomedical Sciences and Pathobiology, Center for Molecular Medicine and Infectious Diseases, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, 24061-0342, Blacksburg, VA, USA

Veterinary microbiology (Netherlands) Aug 25 2002, 88 (2) p189-202, ISSN 0378-1135 Journal Code: 7705469

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Brucella abortus resists the microbicidal mechanisms of macrophages, and the expression of its heat shock proteins (HSPs) such as GroEL, GroES and HtrA may play a role in this resistance. Bacterial HSPs can be very immunogenic, inducing protective immunity in various types of bacterial infections. However, the significance of immune responses directed against B. abortus HSPs in the protection against brucellosis is currently unresolved. To elucidate the role of these proteins in protection against Brucella challenge, individual, divalent or trivalent baculovirus (BV) recombinants of B. abortus GroEL, GroES and/or HtrA were injected into BALB/c mice either as protein-expressing whole cells or as purified proteins. The preparations were given to mice in combination with Freund's or Ribi adjuvant, respectively. In addition, some mice were primed with a **vaccinia** virus-GroEL recombinant, followed by inoculation with purified GroEL-Ribi adjuvant combination. Antibodies were observed against B. abortus GroEL and HtrA, but not against GroES. Cellular immune response was demonstrated by observing significant IFN-gamma release by lymphocytes of mice immunized with the purified HtrA-Ribi adjuvant combination. However, none of the mice inoculated with individual, divalent or trivalent HSP-expressing cells combined with complete Freund's adjuvant or inoculated with purified B. abortus HSPs combined with Ribi adjuvant, were protected against challenge with B. abortus virulent strain 2308. Priming with **vaccinia** virus-GroEL recombinant and boosting with GroEL-Ribi combination did not induce protective immunity. Based on the results obtained, we suggest that although humoral and cell-mediated immune responses are induced, but protective immune response is not induced by B. abortus HSPs.

Tags: Female; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Antibodies, Bacterial--biosynthesis--BI; *Bacterial **Vaccines** --immunology--IM; *Brucella abortus--immunology--IM; *Heat-Shock Proteins--immunology--IM; Animals; Baculoviridae; Brucellosis--prevention and control--PC; **GroEL Protein** --i

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18552494   PMID: 16140966
  Chaperon and adjuvant activity of hsp70: different natural killer
requirement for cross-priming of chaperoned and bystander antigens.
  Massa Chiara; Melani Cecilia; Colombo Mario P
  Immunotherapy and Gene Therapy Unit, Department of Experimental Oncology,
Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy.
  Cancer research (United States)  Sep 1 2005,  65  (17)  p7942-9,  ISSN
0008-5472   Journal Code: 2984705R
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: In Process
  Subfile:   INDEX MEDICUS
  Heat  shock  proteins  (HSP) convey both chaperoned propeptide and danger
signal  to dendritic cells (DC). However, few studies have compared the two
activities.  Using a murine inducible hsp70 secreted by cells distinct from
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Infections--prevention and control--PC; *Yersinia enterocolitica --immunology--IM; Adjuvants, Immunologic--therapeutic use--TU; Animals; Antibodies, Bacterial--blood--BL; Antigens, Bacterial--therapeutic use--TU; Bacterial Vaccines--therapeutic use--TU; Drug Combinations; Evaluation Studies; ISCOMs--ultrastructure--UL; Immunoglobulin G--blood--BL; Lymphocyte Activation; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Spleen--microbiology--MI; T-Lymphocytes--immunology--IM

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Antibodies, Bacterial); 0 (Antigens, Bacterial); 0 (Bacterial Vaccines); 0 (Chaperonin 60); 0 (Drug Combinations); 0 (ISCOMs); 0 (Immunoglobulin G); 187348-17-0 (Interleukin-12)

Record Date Created: 19960926

Record Date Completed: 19960926

25/9/47

DIALOG(R)File 155:MEDLINE(R)

11971597 PMID: 9255766

Immunoprophylactic properties of 71-kDa cell wall-associated protein antigen of Mycobacterium tuberculosis H37Ra.

Dhiman N; Khuller G K

Department of Biochemistry, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Medical microbiology and immunology (GERMANY) Jun 1997, 186 (1) p45-51, ISSN 0300-8584 Journal Code: 0314524

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Proteins associated with the cell wall peptidoglycan (CW-Pr) of Mycobacterium tuberculosis H37Ra were isolated to evaluate their immunoreactivity and immunoprophylactic properties against experimental tuberculosis. Chemical treatment of the cell wall with trifluoromethanesulfonic acid: anisole (2:1) resulted in the release of three proteins of 71, 60 and 45 kDa as resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. A comparative study of immune responses elicited to individual proteins in mice immunized with CW-Pr emulsified in incomplete Freund's adjuvant showed the 71-kDa protein to be the most immunoreactive antigen. This 71-kDa protein was found to cross-react with the 70-kDa **heat shock protein** from M. leprae and possessed ATPase activity. Mice immunized with the 71-kDa protein exhibited significantly higher immune responses, on the basis of T and B cell reactivity, as compared to a M. bovis Bacillus Calmette Guerin (BCG)-**vaccinated** group. The culture supernatants collected from 71-kDa stimulated lymphocytes stimulated exhibited increased interferon-gamma and interleukin-2 production. The **protective efficacy** of the 71-kDa protein in comparison to BCG was determined by challenging the mice with a virulent strain M. tuberculosis H37Rv. The 71-kDa protein was found to be more protective in animals challenged at 8 and 16 weeks post immunization, shown by increased survival rates and decreased viable bacilli counts in the target organs as compared to BCG-vaccinated animals.

Tags: Female; Male; Research Support, Non-U.S. Gov't

Descriptors: *Antigens, Bacterial--immunology--IM; *Bacterial Proteins --immunology--IM; *Bacterial Vaccines--immunology--IM; *Mycobacterium tuberculosis--immunology--IM; Animals; Cell Wall--chemistry--CH; Mice; Molecular Weight

CAS Registry No.: 0 (Antigens, Bacterial); 0 (Bacterial Proteins); 0

Menoret A; Chandawarkar R Y; Srivastava P K
Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT 06030, USA.
Immunology (ENGLAND) Nov 2000, 101 (3) p364-70, ISSN 0019-2805 Journal Code: 0374672
Contract/Grant No.: CA44786; CA; NCI; CA64394; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Immunization of mice with cognate cancer-derived **heat - shock protein (hsp)** preparations leads to **protection** from cancer growth. As **hsp** used for **vaccination** or therapy are derived from autologous cancers, **questions** of pathological autoimmunity are of immense significance for the ongoing translation of this approach to therapy of human cancer. Employing the sera of normal adult mice as the first antibody, highly sensitive immunoblotting revealed the presence of anti- **hsp** natural autoantibodies in healthy animals. Natural autoantibodies of the immunoglobulin D (IgD) isotype bind to gp96, whereas **hsp70** was recognized by IgD and IgM autoantibodies. Neither **hsp** was recognized by the IgA, IgE or IgG immunoglobulins contained in the serum. The antigen-antibody recognition was titratable and dependent on the integrity of the IgD molecule. Sera from only a subset of the animals tested were found to be positive for autoantibodies against gp96 and hsp70, and individual and strain-specific variations were detected. Injection of gp96 into healthy mice did not show sustained or consistent anti-gp96 IgD antibody response, class switching, toxicity or pathological autoimmunity. IgD autoantibodies against gp96 and hsp70 were also not detected in the autoimmune lpr mice. These observations show the existence of a measured and tightly regulated natural immune response to hsp.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.
Descriptors: *Antigens, Neoplasm--immunology--IM; *Autoantibodies--blood --BL; *Heat-Shock Proteins 70--immunology--IM; *Immunotherapy, Active --methods--MT; Animals; Autoimmunity; Diabetes Mellitus, Experimental --immunology--IM; Diabetes Mellitus, Type 1--immunology--IM; Immunoglobulin D--blood--BL; Immunoglobulin M--blood--BL; Mice; Mice, Inbred NOD; Mice, Inbred Strains; Species Specificity
CAS Registry No.: 0 (Antigens, Neoplasm); 0 (Autoantibodies); 0 (Heat-Shock Proteins 70); 0 (Immunoglobulin D); 0 (Immunoglobulin M); 0 (sarcoma glycoprotein gp96 rejection antigens)
Record Date Created: 20001208
Record Date Completed: 20001222

25/9/38
DIALOG(R)File 155:MEDLINE(R)

13489666 PMID: 10456921
Isolation of recombinant protective Helicobacter pylori antigens.
Hocking D; Webb E; Radcliff F; Rothel L; Taylor S; Pinczower G; Kapouleas C; Braley H; Lee A; Doidge C
Research and Development Division, CSL Limited, Parkville, Victoria, Australia 3052.
Infection and immunity (UNITED STATES) Sep 1999, 67 (9) p4713-9, ISSN 0019-9567 Journal Code: 0246127
Publishing Model Print

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

A total of seven clones producing both new and previously described Helicobacter pylori proteins were isolated from a library of H. pylori genomic DNA. The screening approach by which these proteins were detected relied on the use of antisera raised in mice **vaccinated** with Helicobacter felis sonicate plus cholera toxin, a regimen which **protects** mice from H. pylori challenge. This strategy was designed to maximize the possibility of obtaining antigens which might be capable of conferring **protection** from H. pylori infection. Two of the clones were shown to encode the urease enzyme and the **heat shock protein HspB** , which have already been identified as **protective** antigens. The other five clones were sequenced, protein coding regions were deduced, and these sequences were amplified by PCR for incorporation into Escherichia coli expression vectors. The proteins produced from these expression systems were purified to allow testing for **protective efficacy** in an H. pylori mouse model. All five proteins were able to facilitate the clearance of a challenge with H. pylori, as judged by an assay of gastric urease activity and light microscopy on stomach sections. These results clearly indicate that the screening strategy has successfully identified candidate **vaccine** antigens.

Tags: Research Support, Non-U.S. Gov't

Descriptors: *Antigens, Bacterial--genetics--GE; *Helicobacter pylori --genetics--GE; Animals; Antigens, Bacterial--immunology--IM; Antigens, Bacterial--isolation and purification--IP; Base Sequence; DNA, Bacterial; Gene Expression; Genome, Bacterial; Genomic Library; Helicobacter Infections--prevention and control--PC; Helicobacter pylori--immunology--IM ; Mice; Molecular Sequence Data; Recombination, Genetic; Sequence Analysis, DNA; Urease--genetics--GE

Molecular Sequence Databank No.: GENBANK/U86607; GENBANK/U86608; GENBANK/U86609; GENBANK/U86610

CAS Registry No.: 0 (Antigens, Bacterial); 0 (DNA, Bacterial)

Enzyme No.: EC 3.5.1.5 (Urease)

Record Date Created: 19991005

Record Date Completed: 19991005

25/9/37

DIALOG(R)File 155:MEDLINE(R)

13702322 PMID: 11349057

Immunogenicity and protective efficacy **of a Plasmodium yoelii** Hsp60 **DNA** vaccine **in BALB/c mice.**

Sanchez G I; Sedegah M; Rogers W O; Jones T R; Sacci J; Witney A; Carucci D J; Kumar N; Hoffman S L

Malaria Program, Naval Medical Research Center, Silver Spring, Maryland 20910-7500, USA.

Infection and immunity (United States) Jun 2001, 69 (6) p3897-905, ISSN 0019-9567 Journal Code: 0246127

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The gene encoding the 60-kDa **heat shock protein** of Plasmodium

yoelii (PyHsp60) was cloned into the VR1012 and VR1020 mammalian expression vectors. Groups of 10 BALB/c mice were immunized intramuscularly at 0, 3, and 9 weeks with 100 microg of PyHsp60 DNA **vaccine** alone or in combination with 30 microg of pmurGMCSF. Sera from immunized mice but not from vector control groups recognized P. yoelii sporozoites, liver stages, and infected erythrocytes in an indirect fluorescent antibody test. Two weeks after the last immunization, mice were challenged with 50 P. yoelii sporozoites. In one experiment the **vaccine** pPyHsp60-VR1012 used in combination with pmurGMCSF gave 40% **protection** (Fisher's exact test; P = 0.03, vaccinated versus control groups). In a second experiment this vaccine did not protect any of the immunized mice but induced a delay in the onset of parasitemia. In neither experiment was there any evidence of a protective effect against the asexual erythrocytic stage of the life cycle. In a third experiment mice were primed with PyHsp60 DNA, were boosted 2 weeks later with 2 x 10(3) irradiated P. yoelii sporozoites, and were challenged several weeks later. The presence of PyHsp60 in the immunization regimen did not lead to reduced blood-stage infection or development of parasites in hepatocytes. PyHsp60 DNA vaccines were immunogenic in BALB/c mice but did not consistently, completely protect against sporozoite challenge. The observation that in some of the PyHsp60 DNA vaccine-immunized mice there was protection against infection or a delay in the onset of parasitemia after sporozoite challenge deserves further evaluation.

Tags: Female; Research Support, Non-U.S. Gov't

Descriptors: *Antibodies, Protozoan--blood--BL; *Chaperonin 60 --immunology--IM; *Malaria--prevention and control--PC; *Malaria Vaccines --immunology--IM; *Plasmodium yoelii--immunology--IM; *Vaccines, DNA --immunology--IM; Animals; Antigens, Protozoan--immunology--IM; Chaperonin 60--genetics--GE; Chaperonin 60--metabolism--ME; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; Granulocyte-Macrophage Colony-Sti mulating Factor--metabolism--ME; Immunization; Immunization Schedule; Malaria--immunology--IM; Mice; Mice, Inbred BALB C; Plasmids--genetics--GE

CAS Registry No.: 0 (Antibodies, Protozoan); 0 (Antigens, Protozoan); 0 (Chaperonin 60); 0 (Malaria Vaccines); 0 (Plasmids); 0 (Vaccines, DNA); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

Record Date Created: 20010511

Record Date Completed: 20010628

25/9/35

DIALOG(R)File 155:MEDLINE(R)

13820870 PMID: 11490008

V beta 6+ T cells are obligatory for vaccine-induced immunity to Histoplasma capsulatum.

Deepe G S; Gibbons R

Division of Infectious Diseases, University of Cincinnati College of Medicine, and Veterans Affairs Hospital, Cincinnati, OH 45267, USA. george.deepe@uc.edu

Journal of immunology (Baltimore, Md. - 1950) (United States) Aug 15 2001, 167 (4) p2219-26, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: AI34361; AI; NIAID; AI42747; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

We examined TCR usage to a **protective** fragment of **heat shock protein** 60 from the fungus, Histoplasma capsulatum. Nearly 90% of T cell

clones from C57BL/6 mice **vaccinated** with this protein were Vbeta6+; the remainder were Vbeta14+. Amino acid motifs of the CDR3 region from Vbeta6+ cells were predominantly IxGGG, IGG, or SxxGG, whereas it was uniformly SFSGG for Vbeta14+ clones. Short term T cell lines from Vbeta6+-depleted mice **failed** to recognize Ag, and no T cell clones could be generated. To determine whether Vbeta6+ cells were functionally important, we eliminated them during **vaccination** . Depletion of Vbeta6+ cells abrogated **protection** in vivo and upon adoptive transfer of cells into TCR alphabeta(-/-) mice. Transfer of a Vbeta6+, but not a Vbeta14+, clone into TCR alphabeta(-/-) mice prolonged survival. Cytokine generation by Ag-stimulated splenocytes from immunized mice depleted of Vbeta6+ cells was similar to that of controls. The **efficacy** of the Vbeta6+ clone was associated with elevated production of IFN-gamma, TNF-alpha, and GM-CSF compared with that of the Vbeta14+ clone. More Vbeta6+ cells were present in lungs and spleens of TCR alphabeta(-/-) on day 3 postinfection compared with Vbeta14+ cells. Thus, a single Vbeta family was essential for vaccine-induced immunity. Moreover, the mechanism by which Vbeta6+ contributed to protective immunity differed between unfractionated splenocytes and T cell clones.

Tags: Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Fungal Vaccines--immunology--IM; *Histoplasma--immunology --IM; *Histoplasmosis--immunology--IM; *Receptors, Antigen, T-Cell, alpha-beta--biosynthesis--BI; *T-Lymphocyte Subsets--immunology--IM; *T-Lymphocyte Subsets--metabolism--ME; Adoptive Transfer; Animals; Base Sequence; Cell Line; Chaperonin 60--immunology--IM; Clone Cells --transplantation--TR; Cytokines--analysis--AN; Cytokines--biosynthesis --BI; Fungal Vaccines--administration and dosage--AD; Histoplasmosis --prevention and control--PC; Injections, Intravenous; Injections, Subcutaneous; Lymphocyte Depletion; Mice; Mice, Inbred C57BL; Mice, Knockout; Peptide Fragments--administration and dosage--AD; Peptide Fragments--immunology--IM; Protein Structure, Tertiary; Receptors, Antigen, T-Cell, alpha-beta--deficiency--DF; Receptors, Antigen, T-Cell, alpha-beta --genetics--GE; Spleen--cytology--CY; Spleen--transplantation--TR; T-Lymphocyte Subsets--transplantation--TR

CAS Registry No.: 0 (Chaperonin 60); 0 (Cytokines); 0 (Fungal Vaccines); 0 (Peptide Fragments); 0 (Receptors, Antigen, T-Cell, alpha-beta)

Record Date Created: 20010807

Record Date Completed: 20011205

25/9/33

DIALOG(R)File 155:MEDLINE(R)

13881569 PMID: 11566370

Molecular and immunological characterisation of the glucose regulated protein 78 of Leishmania donovani(1).

Jensen A T; Curtis J; Montgomery J; Handman E; Theander T G

Centre for Medical Parasitology, Institue for Medical Microbiology and Immunology, University of Copenhagen, The Panum Institute, Denmark. atjr@biobase.dk

Biochimica et biophysica acta (Netherlands) Sep 10 2001, 1549 (1) p73-87, ISSN 0006-3002 Journal Code: 0217513

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

To identify novel potential Leishmania **vaccine** antigens, antibodies

from patients with visceral leishmaniasis (VL) were used to isolate clones from a cDNA expression library of L. donovani amastigotes. Glucose Regulated Protein (GRP78), a member of the 70 kDa **heat - shock protein** family was identified and characterised. The GRP78 gene was localised to chromosome 15 in L. donovani, L. major, and L. mexicana by pulse-field gel electrophoresis. The Leishmania GRP78 protein contain a carboxy-terminal endoplasmic reticulum retention signal sequence (MDDL) as does the Trypanosoma cruzi GRP78. Immunofluorescence using antibodies to the recombinant DNA-derived GRP78 protein showed staining localised to reticular material throughout the cytoplasm and in the perinuclear region of promastigotes, suggesting that the protein is localised in the endoplasmic reticulum. The **protective efficacy** of GRP78 was assessed in mice **vaccine** experiments. A GRP78 DNA **vaccine** primed for an immune response that **protected** C57Bl/6 and C3H/He mice against infection with L. major. Similarly vaccination with a recombinant form of GRP78 purified from Escherichia coli and administered with Freund's as adjuvant induced protective immunity in C57Bl/6 mice.

Tags: Research Support, Non-U.S. Gov't

Descriptors: *Leishmania donovani--metabolism--ME; *Protozoan Proteins --metabolism--ME; *Protozoan Vaccines--immunology--IM; Amino Acid Sequence; Animals; Antigens, Protozoan--immunology--IM; Base Sequence; Blotting, Northern; Cloning, Molecular; Disease Models, Animal; Electrophoresis, Gel, Pulsed-Field; Gene Library; Genes, Protozoan; Heat-Shock Proteins--genetics --GE; Heat-Shock Proteins--immunology--IM; Heat-Shock Proteins --metabolism--ME; Humans; Leishmania donovani--genetics--GE; Leishmania donovani--immunology--IM; Leishmaniasis--immunology--IM; Mice; Mice, Inbred C3H; Mice, Inbred C57BL; Microscopy, Confocal; Molecular Sequence Data; Protozoan Proteins--genetics--GE; Protozoan Proteins--immunology--IM; Protozoan Vaccines--administration and dosage--AD; Vaccination; Vaccines, DNA--administration and dosage--AD

Molecular Sequence Databank No.: GENBANK/AF322906

CAS Registry No.: 0 (Antigens, Protozoan); 0 (Heat-Shock Proteins); 0 (Protozoan Proteins); 0 (Protozoan Vaccines); 0 (Vaccines, DNA); 0 (glucose regulated protein 78, protozoan)

Record Date Created: 20010921

Record Date Completed: 20011018

25/9/32

DIALOG(R)File 155:MEDLINE(R)

14103748 PMID: 11880222

Recombinant Mycobacterium bovis BCG producing the circumsporozoite protein of Plasmodium falciparum FCC-1/HN strain induces strong immune responses in BALB/c mice.

Zheng Chunfu; Xie Peimei; Chen Yatang

Institute of Infectious and Parasitic Diseases, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, PR China. zhengc@sask.usask.ca

Parasitology international (Netherlands) Mar 2002, 51 (1) p1-7, ISSN 1383-5769 Journal Code: 9708549

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The current **vaccine** against tuberculosis, Mycobacterium bovis strain bacillus Calmette-Guerin (BCG), offers potential advantages as a live,

innately immunogenic **vaccine** vehicle for expression and delivery of **protective** recombinant antigens. Malaria is one of the severest parasitic diseases in humans especially in the developing world. No **efficacious** **vaccine** is currently available. However, circumsporozoite protein (CSP) is a malaria **vaccine** candidate currently undergoing clinical trials. We analyzed the immune response to recombinant BCG (rBCG) **vaccine** expressing Plasmodium falciparum CSP (BCG-CSP) under the control of **heat shock** **protein** 70 promoter in BALB/c mice. The lymphocytes proliferative response to P. falciparum soluble antigen was significantly higher than those in the groups of BCG and normal saline, and the production of cytokines (IFN-gamma and IL-2) in response to malaria antigen was significantly higher in rBCG and BCG groups than control group of normal saline. A specific IgG antibody response against P. falciparum antigen of CSP was also characterized. The booster injection could enhance the production of cytokine, proliferation responses of spleen lymphocytes and the antibodies titer of BCG-CSP. The results in the study demonstrated that rBCG **vaccine** producing CSP is an appropriate vaccine for further evaluation in non-human primates.

Tags: Research Support, Non-U.S. Gov't

Descriptors: *Malaria Vaccines--immunology--IM; *Malaria, Falciparum --prevention and control--PC; *Mycobacterium bovis--genetics--GE; *Protozoan Proteins--immunology--IM; *Vaccines, Synthetic--immunology--IM; Animals; Antibodies, Protozoan--blood--BL; Interferon Type II--biosynthesis --BI; Interleukin-2--biosynthesis--BI; Lymphocyte Activation--immunology --IM; Lymphocyte Subsets; Mice; Mice, Inbred BALB C; Mycobacterium bovis --immunology--IM; Plasmodium falciparum--immunology--IM; Protozoan Proteins --genetics--GE

CAS Registry No.: 0 (Antibodies, Protozoan); 0 (Interleukin-2); 0 (Malaria Vaccines); 0 (Protozoan Proteins); 0 (Vaccines, Synthetic); 0 (circumsporozoite protein, Protozoan); 82115-62-6 (Interferon Type II)

Record Date Created: 20020306

Record Date Completed: 20020611

25/9/31

DIALOG(R)File 155:MEDLINE(R)

14259279 PMID: 12065519

Cellular and molecular regulation of vaccination with heat shock protein 60 from Histoplasma capsulatum.

Deepe George S; Gibbons Reta S

Veterans Affairs Hospital and Division of Infectious Diseases, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267-0560, USA. george.deepe@uc.edu

Infection and immunity (United States) Jul 2002, 70 (7) p3759-67, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI-34361; AI; NIAID; AI-42737; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Vaccination with **heat shock protein** 60 (**Hsp60**) from Histoplasma capsulatum induces a protective immune response in mice. We explored the cellular and molecular requirements for the efficacy of recombinant **Hsp60** in mice. Depletion of CD4(+), but not CD8(+), cells during the inductive phase of **vaccination** abolished protection, as assessed by survival and by the fungal burden in lungs and spleens. In the expressive phase, the

elimination of CD4(+) or CD8(+) cells after immunization did not significantly alter fungal recovery or survival from a lethal challenge. Depletion of both subpopulations after **Hsp60 vaccination** resulted in a failure to control a lethal infection and a higher fungal burden in lungs and spleens. Cytokine release by spleen cells from mice **vaccinated** with **Hsp60** produced substantially more gamma interferon and interleukin-10 and -12 than that of cells from mice immunized with either H. capsulatum recombinant **Hsp70** or bovine serum albumin. The generation of gamma interferon, but not of interleukin-10, was dependent on T cells, in particular CD4(+) cells. Treatment of **Hsp60** -immunized mice with monoclonal antibody to gamma interferon or interleukin-10 or -12 in the inductive phase of **vaccination** was accompanied by increased recovery of yeast cells from lungs and spleens and 100% mortality. Likewise, the neutralization of gamma interferon or interleukin-12 abolished the **protective** effect of **Hsp60** in the expressive phase. These results delineate the complexity of the regulatory elements necessary for **vaccination** against this fungus.

Tags: Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Antigens, Fungal--immunology--IM; *Chaperonin 60 --immunology--IM; *Fungal Vaccines--immunology--IM; *Histoplasmosis --immunology--IM; *Vaccines, Synthetic--immunology--IM; Animals; CD4-Positive T-Lymphocytes--immunology--IM; CD8-Positive T-Lymphocytes --immunology--IM; Disease Models, Animal; Histoplasma--immunology--IM; Interferon Type II--immunology--IM; Interleukin-10--immunology--IM; Interleukin-12--immunology--IM; Interleukin-4--immunology--IM; Mice; Mice, Inbred C57BL; Mice, Nude; Spleen--cytology--CY; Spleen--immunology--IM; Tumor Necrosis Factor-alpha--immunology--IM; Vaccination

CAS Registry No.: 0 (Antigens, Fungal); 0 (Chaperonin 60); 0 (Fungal Vaccines); 0 (Tumor Necrosis Factor-alpha); 0 (Vaccines, Synthetic); 130068-27-8 (Interleukin-10); 187348-17-0 (Interleukin-12); 207137-56-2 (Interleukin-4); 82115-62-6 (Interferon Type II)

Record Date Created: 20020614

Record Date Completed: 20020730

25/9/30

DIALOG(R)File 155:MEDLINE(R)

14304506 PMID: 12117930

Immunization with a polyprotein vaccine **consisting of the T-Cell antigens thiol-specific antioxidant, Leishmania major** stress **-inducible** protein **1, and Leishmania elongation initiation factor** protects **against leishmaniasis.**

Coler Rhea N; Skeiky Yasir A W; Bernards Karen; Greeson Kay; Carter Darrick; Cornellison Charisa D; Modabber Farrokh; Campos-Neto Antonio; Reed Steven G

Infectious Disease Research Institute, Seattle, Washington 98104, USA. coler@idri.org

Infection and immunity (United States) Aug 2002, 70 (8) p4215-25, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI25038; AI; NIAID; AI36810; AI; NIAID; GM08347; GM; NIGMS

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Development of an effective **vaccine** against Leishmania infection is a priority of tropical disease research. We have recently demonstrated **protection** against Leishmania major in the murine and nonhuman primate models with individual or combinations of purified leishmanial recombinant antigens delivered as plasmid DNA constructs or formulated with recombinant interleukin-12 (IL-12) as adjuvant. In the present study, we immunized BALB/c mice with a recombinant polyprotein comprising a tandem fusion of the leishmanial antigens thiol-specific antioxidant, L. major **stress** -inducible **protein** 1 (LmSTI1), and Leishmania elongation initiation factor (LeIF) delivered with adjuvants suitable for human use. Aspects of the safety, immunogenicity, and **vaccine efficacy** of formulations with each individual component, as well as the polyprotein referred to as Leish-111f, were assessed by using the L. major challenge model with BALB/c mice. No adverse reactions were observed when three subcutaneous injections of the Leish-111f polyprotein formulated with either MPL-squalene (SE) or Ribi 529-SE were given to BALB/c mice. A predominant Th1 immune response characterized by in vitro lymphocyte proliferation, gamma interferon production, and immunoglobulin G2A antibodies was observed with little, if any, IL-4. Moreover, Leish-111f formulated with MPL-SE conferred immunity to leishmaniasis for at least 3 months. These data demonstrate success at designing and developing a prophylactic leishmaniasis vaccine that proved effective in a preclinical model using multiple leishmanial antigens produced as a single protein delivered with a powerful Th1 adjuvant suitable for human use.

Tags: Female; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Antigens, Protozoan--immunology--IM; *Antioxidants; *Heat-Shock Proteins--immunology--IM; *Leishmania major--immunology--IM; *Leishmania mexicana--immunology--IM; *Leishmaniasis, Cutaneous--prevention and control--PC; *Lipid A--analogs and derivatives--AA; *Molecular Chaperones--immunology--IM; *Peptide Initiation Factors--immunology--IM; *Peroxidases--immunology--IM; *Polyproteins--immunology--IM; *Protozoan Proteins; *Protozoan Vaccines--immunology--IM; *Vaccines, Synthetic --immunology--IM; Adjuvants, Immunologic; Animals; Antigens, Protozoan --genetics--GE; Cell Wall Skeleton; Cord Factors; Disease Models, Animal; Heat-Shock Proteins--genetics--GE; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Molecular Chaperones--genetics--GE; Peptide Initiation Factors --genetics--GE; Peroxidases--genetics--GE; Polyproteins--genetics--GE; Protozoan Vaccines--genetics--GE; T-Lymphocytes--immunology--IM; Vaccinatio n; Vaccines, Synthetic--genetics--GE

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Antigens, Protozoan) ; 0 (Antioxidants); 0 (Cell Wall Skeleton); 0 (Cord Factors); 0 (Heat-Shock Proteins); 0 (LeIF protein, Leishmania); 0 (Lipid A); 0 (Molecular Chaperones); 0 (Peptide Initiation Factors); 0 (Polyproteins); 0 (Protozoan Proteins); 0 (Protozoan Vaccines); 0 (Ribi adjuvant); 0 (Stip1 protein, mouse); 0 (Vaccines, Synthetic); 0 (monophosphoryl lipid A)

Enzyme No.: EC 1.- (alkyl hydroperoxide reductase); EC 1.11.1. (Peroxidases)

Record Date Created: 20020715

Record Date Completed: 20020904

25/9/23

DIALOG(R)File 155:MEDLINE(R)

14824041 PMID: 12794147

Proteins and their derived peptides as carriers in a conjugate vaccine for Streptococcus pneumoniae: self-heat shock protein 60 and tetanus

toxoid.

Amir-Kroll Hila; Nussbaum Gabriel; Cohen Irun R

Department of Immunology, The Weizmann Institute of Science, Rehovot, Israel.

Journal of immunology (Baltimore, Md. - 1950) (United States) Jun 15 2003, 170 (12) p6165-71, ISSN 0022-1767 Journal Code: 2985117R

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

We induced T cell help for **vaccination** against Streptococcus pneumoniae (Pn) using self and foreign peptides and their source proteins conjugated to the capsular polysaccharide (CPS) of type 4 Pn; the carriers were self- **heat shock protein** 60 (**HSP60**) and tetanus toxoid (TT). We measured the production of IgG Abs to the CPS and the carriers, and tested resistance to challenge with highly lethal amounts of Pn injected i.p. (LD(50) x 10(3)-10(6)). We now report that **vaccination protects** old and young mice from bacterial challenge; however, there were significant differences in **vaccine efficacy** based on the carrier. Self- **HSP60** peptide p458m was more effective than the whole **HSP60** molecule and was equally effective compared with TT. Both p458m and TT were more **protective** than the TT-derived peptide p30 after a single **vaccination** . However, peptide p30 was effective in more MHC genotypes than was p458m. Unlike other **vaccines** , **protection** conferred by p458m was not related to the amount of anti-CPS Ab: mice that produced very little Ab were still **protected** from highly lethal doses of bacteria (LD(50) x 10(5)-10(6)). Furthermore, unlike the other carriers, there was no Ab response to the p458m carrier. Thus, peptides, self as well as foreign, can provide T cell help that differs functionally from that provided by the whole parent protein.

Tags: Comparative Study; Female; Research Support, Non-U.S. Gov't

Descriptors: *Carrier Proteins--immunology--IM; *Chaperonin 60 --immunology--IM; *Peptide Fragments--immunology--IM; *Pneumococcal Vaccines--immunology--IM; *Tetanus Toxoid--immunology--IM; Age Factors; Amino Acid Sequence; Animals; Autoantibodies--biosynthesis--BI; Autoantigens--administration and dosage--AD; Autoantigens--immunology--IM; Autoantigens--therapeutic use--TU; Carrier Proteins--administration and dosage--AD; Carrier Proteins--therapeutic use--TU; Chaperonin 60 --administration and dosage--AD; Chaperonin 60--therapeutic use--TU; Dose-Response Relationship, Immunologic; Immunization Schedule; Immunoglobulin G--biosynthesis--BI; Injections, Subcutaneous; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Molecular Sequence Data; Peptide Fragments--administration and dosage--AD; Peptide Fragments--therapeutic use--TU; Pneumococcal Infections--immunology--IM; Pneumococcal Infections --prevention and control--PC; Pneumococcal Vaccines--administration and dosage--AD; Pneumococcal Vaccines--therapeutic use--TU; Polysaccharides, Bacterial--administration and dosage--AD; Polysaccharides, Bacterial --immunology--IM; Polysaccharides, Bacterial--therapeutic use--TU; Species Specificity; Tetanus Toxoid--administration and dosage--AD; Tetanus Toxoid --therapeutic use--TU; Vaccines, Conjugate--administration and dosage--AD; Vaccines, Conjugate--immunology--IM; Vaccines, Conjugate--therapeutic use --TU

CAS Registry No.: 0 (Autoantibodies); 0 (Autoantigens); 0 (Carrier Proteins); 0 (Chaperonin 60); 0 (Immunoglobulin G); 0 (Peptide Fragments); 0 (Pneumococcal Vaccines); 0 (Polysaccharides, Bacterial); 0 (Tetanus Toxoid); 0 (Vaccines, Conjugate); 0 (pneumonococcal polysaccharide, type 4)

Record Date Created: 20030609

Record Date Completed: 20030908

25/9/22
DIALOG(R)File 155:MEDLINE(R)

14879224 PMID: 12860174
Adjuvants for vaccines, a quest.
Audibert Francoise
22 rue EMERIAU, 75015 Paris, France. Keroustad@aol.com
International immunopharmacology (Netherlands) Aug 2003, 3 (8) p1187-93, ISSN 1567-5769 Journal Code: 100965259
Publishing Model Print
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Efficient vaccines comprise a specific moiety: the structures presenting the protective antigenic determinants, and a nonspecific moiety: the adjuvant components. Dramatic advances have been reported concerning the specific moiety and new and highly purified immunogens have been defined and prepared. The use of vaccines is no longer restricted to the prevention of infections, they are now considered as therapeutic tools especially in cancer immunotherapy. In contrast, alum is still the only adjuvant suitable for clinical application. The success of the new avenues opened in vaccinology depends on the availability of appropriate immunomodulating preparations. For each given type of **vaccine** , the optimal profile of activity of the adjuvant moiety has to be defined, according to the response required to provide **protection** or cure. Thus, it is urgent to design and develop adjuvants active not only on the humoral responses but also on the cellular immune responses. This adjuvant function must have the capacity of turning on the innate responses, which play a decisive and instructive role in emanating the adaptive immune responses. These considerations encourage one to finalize immunomodulating procedures rather than to look only for new adjuvant compounds. Manipulations of dendritic cells (DCs), use of heat-shock proteins (**HSPs**) as carriers endowed of adjuvant activity or introduction of varying immunostimulating motives in genetic **vaccines** represent examples illustrating this new rationale. (54 Refs.)
Descriptors: *Adjuvants, Immunologic--therapeutic use--TU; *Vaccines --therapeutic use--TU; Animals; Communicable Diseases--drug therapy--DT; Communicable Diseases--immunology--IM; Dendritic Cells--immunology--IM; Heat-Shock Proteins--immunology--IM; Humans; Immunity, Cellular --drug effects--DE; Neoplasms--drug therapy--DT; Neoplasms--immunology--IM; Vaccines, DNA--therapeutic use--TU
CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Heat-Shock Proteins) ; 0 (Vaccines); 0 (Vaccines, DNA)
Record Date Created: 20030715
Record Date Completed: 20040329

25/9/21
DIALOG(R)File 155:MEDLINE(R)

14937245 PMID: 12933831
A DNA prime-Mycobacterium bovis BCG boost vaccination strategy for cattle induces protection against bovine tuberculosis.

Skinner Margot A; Buddle Bryce M; Wedlock D Neil; Keen Denise; de Lisle Geoffrey W; Tascon Ricardo E; Ferraz Jose Candido; Lowrie Douglas B; Cockle Paul J; Vordermeier H Martin; Hewinson R Glyn

AgResearch, Wallaceville Animal Research Centre, Upper Hutt, New Zealand. margot.skinner@agresearch.co.nz

Infection and immunity (United States) Sep 2003, 71 (9) p4901-7, ISSN 0019-9567 Journal Code: 0246127

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The variable **efficacy** of bacillus Calmette-Guerin (Mycobacterium bovis BCG) in **protecting** humans and cattle against tuberculosis has prompted a search for a more effective **vaccination** regimen. A prime-boost strategy was investigated in cattle naturally sensitized to environmental mycobacteria by using a combination of three DNA **vaccines** coding for **Hsp** 65, **Hsp** 70, and Apa for priming, followed by a boost with BCG prior to experimental challenge with virulent M. bovis. Controls were **vaccinated** with DNA or BCG alone or were not **vaccinated** . The immune responses were monitored throughout the study, and **protection** was assessed based on reductions in the numbers of lesions and viable mycobacteria in lymph node samples. **Vaccination** with BCG alone or with a DNA prime-BCG boost regimen induced high levels of antigen-specific gamma interferon (IFN-gamma) in whole-blood cultures. In the prime-boost group there were fewer animals with severe lung lesions, fewer lymph nodes with lesions per animal, a smaller proportion of animals with lesions, lower mean lung and lymph node lesion scores, and less M. bovis isolated from retropharyngeal and thoracic lymph nodes compared to the results obtained for the nonvaccinated animals. The prime-boost regimen induced significant enhancement of protection in six parameters, compared with significant enhancement of protection in only two parameters for BCG alone. In addition, following challenge, in vitro IFN-gamma responses against ESAT-6 and CFP-10, as well as bovine tuberculin-induced skin test and in vitro IFN-gamma responses, were identified as immunological markers that predicted protection. The use of the prime-boost strategy suggested that a combination of vaccines may be better than a single vaccine for protection against tuberculosis.

Tags: Female; In Vitro; Research Support, Non-U.S. Gov't

Descriptors: *BCG Vaccine--administration and dosage--AD; *Tuberculosis, Bovine--prevention and control--PC; *Vaccines, DNA --administration and dosage--AD; Animals; BCG Vaccine--genetics--GE; Base Sequence; Birds; Cattle; Colony Count, Microbial; DNA Primers--genetics--GE; Humans; Immunization, Secondary; Interferon Type II--biosynthesis--BI; Interleukin-2--biosynthesis--BI; Mycobacterium bovis--genetics--GE; Mycobacterium bovis--immunology--IM; Mycobacterium bovis--isolation and purification--IP; T-Lymphocytes--immunology--IM; Tuberculin--pharmacology --PD; Tuberculosis, Bovine--immunology--IM; Tuberculosis, Bovine --microbiology--MI; Tuberculosis, Bovine--pathology--PA; Vaccines, DNA --genetics--GE

CAS Registry No.: 0 (BCG Vaccine); 0 (DNA Primers); 0 (Interleukin-2); 0 (Tuberculin); 0 (Vaccines, DNA); 82115-62-6 (Interferon Type II)

Record Date Created: 20030822

Record Date Completed: 20030929

25/9/19

Vaccine (Netherlands) Dec 8 2003, 22 (1) p49-56, ISSN 0264-410X Journal Code: 8406899
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

A DNA **vaccine** codifying the mycobacterial **hsp65** can prevent infection with Mycobacterium tuberculosis in a prophylactic setting and also therapeutically reduce the number of bacteria in infected mice. The **protective** mechanism is thought to be related to Th1-mediated events that result in bacterial **killing** . To determine the best method of **hsp65** introduction for **vaccination** **efficacy** against tuberculosis (TB), we evaluated the immunogenicity and **protection** of DNA- **hsp65** administered by gene gun bombardment or intramuscular (i.m.) injection of naked DNA. Immunization by gene gun induced immune response with plasmid doses 100-fold lower than those required for intramuscular immunization. However, in contrast to intramuscular immunization, which was protective in these studies, gene gun immunization did not protect BALB/c mice against challenge infection.

Tags: Female; Research Support, Non-U.S. Gov't
Descriptors: *Bacterial Proteins--immunology--IM; *Chaperonins --immunology--IM; *DNA, Bacterial--biosynthesis--BI; *Tuberculosis Vaccines --immunology--IM; *Vaccines, DNA--immunology--IM; Animals; Antibodies, Bacterial--analysis--AN; Antibodies, Bacterial--biosynthesis--BI; Biolistics; Cytokines--biosynthesis--BI; DNA, Bacterial--genetics--GE; DNA, Bacterial--immunology--IM; Gold; Injections, Intramuscular; Mice; Mice, Inbred BALB C; Microspheres
CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Bacterial Proteins); 0 (Chaperonins); 0 (Cytokines); 0 (DNA, Bacterial); 0 (Tuberculosis Vaccines); 0 (Vaccines, DNA); 0 (heat-shock protein 65, Mycobacterium); 7440-57-5 (Gold)
Record Date Created: 20031107
Record Date Completed: 20040408

25/9/11
DIALOG(R)File 155:MEDLINE(R)

16396074 PMID: 15557616

A heterologous DNA priming-Mycobacterium bovis BCG boosting immunization strategy using mycobacterial Hsp70, Hsp65, and Apa antigens improves protection against tuberculosis in mice.

Ferraz Jose C; Stavropoulos Evangelos; Yang Min; Coade Steve; Espitia Clara; Lowrie Douglas B; Colston M Joseph; Tascon Ricardo E
The National Institute for Medical Research, Mill Hill, London NW7 1AA, United Kingdom. tricard@nimr.mrc.ac.uk

Infection and immunity (United States) Dec 2004, 72 (12) p6945-50, ISSN 0019-9567 Journal Code: 0246127
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Tuberculosis is responsible for >2 million deaths a year, and the number of new cases is rising worldwide. DNA **vaccination** combined with Mycobacterium bovis bacillus Calmette Guerin (BCG) represents a potential

strategy for prevention of this disease. Here, we used a heterologous prime-boost immunization approach using a combination of DNA plasmids and BCG in order to improve the **efficacy** of **vaccination** against Mycobacterium tuberculosis infection in mice. As model antigens, we selected the M. tuberculosis Apa (for alanine-proline-rich antigen) and the immunodominant **Hsp65** and **Hsp70** mycobacterial antigens combined with BCG. We demonstrated that animals injected with a combination of DNA vectors expressing these antigens, when boosted with BCG, showed increased specific antimycobacterial immune responses compared to animals **vaccinated** with BCG alone. More importantly, the **protection** achieved with this regimen was also significantly better than with BCG alone.

Tags: Female; Research Support, Non-U.S. Gov't

Descriptors: *Antigens, Bacterial--immunology--IM; *BCG Vaccine --immunology--IM; *Bacterial Proteins--immunology--IM; *Chaperonins --immunology--IM; *Heat-Shock Proteins 70--immunology--IM; *Tuberculosis --prevention and control--PC; *Vaccines, DNA--immunology--IM; Animals; CD4-Positive T-Lymphocytes--immunology--IM; CD8-Positive T-Lymphocytes --immunology--IM; Immunization, Secondary; Interferon Type II--biosynthesis --BI; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL

CAS Registry No.: 0 (Antigens, Bacterial); 0 (BCG Vaccine); 0 (Bacterial Proteins); 0 (Chaperonins); 0 (HSP70 protein, Mycobacterium tuberculosis); 0 (Heat-Shock Proteins 70); 0 (Vaccines, DNA); 0 (heat-shock protein 65, Mycobacterium); 144058-44-6 (Mycobacterium tuberculosis antigens); 82115-62-6 (Interferon Type II)

Record Date Created: 20041123

Record Date Completed: 20041230

25/9/12

DIALOG(R)File 155:MEDLINE(R)

16327169 PMID: 15544517

Adjunctive immunotherapy of mycobacterial infections.

Tomioka Haruaki

Department of Microbiology and Immunology, Faculty of Medicine, Shimane University, Izumo, Shimane 693-8501, Japan. tomioka@med.shimane-u.ac.jp

Current pharmaceutical design (Netherlands) 2004, 10 (26) p3297-312, ISSN 1381-6128 Journal Code: 9602487

Publishing Model Print

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

In order to cope with the worldwide increase in the prevalence of multidrug-resistant tuberculosis and Mycobacterium avium complex (MAC) infections, a number of new antimycobacterial drugs have been or are being synthesized and developed. Development of new protocols for chemotherapy of refractory mycobacterioses is also sharing promise. In this context, one promising strategy is to devise regimens to treat patients with refractory mycobacterioses using ordinary antimycobacterial agents in combination with appropriate immunomodulators. This article deals with the following matters: an outline of the host immune response to mycobacterial pathogens, particularly in terms of mobilization of the cytokine network in response to mycobacterial infection, and adjunctive immunotherapy using (1) recombinant immunomodulating cytokines, (especially Th-1 and Th-1-like cytokines such as IFN-gamma, IL-2, IL-12, IL-18 and GM-CSF), (2) inhibitors of immunosuppressive cytokines (TGF-beta) and some proinflammatory tissue-damaging cytokines (TNF-alpha), and (3) immunomodulatory agents such as ATP and its analogs, imidazoquinoline, diethyldithiocarbamate,

poloxamer, dibenzopyran, galactosylceramide, nonsteroidal anti-inflammatory drugs, Chinese traditional medicines, levamisole, synthesized mycobacterial oligoDNA, DNA **vaccine** expressing mycobacterial **HSP65** or IL-12, and heat- **killed** Mycobacterium vaccae. Although adjunctive immunotherapy is fairly **efficacious** in treating intractable mycobacterioses, it still features serious problems and dilemmas, such as high cost, occasionally severe side effects, and, in many cases, only modest **efficacy** in potentiating host defense mechanisms against mycobacterial infections, primarily because of the induction of macrophage-deactivating cytokines during the course of long-term administration of adjunctive agents. (110 Refs.)

Descriptors: *Drug Therapy, Combination; *Immunotherapy--methods--MT; *Mycobacterium Infections--therapy--TH; Animals; Humans; Japan; Models, Biological; Randomized Controlled Trials

Record Date Created: 20041116

Record Date Completed: 20041216

25/9/8

DIALOG(R)File 155:MEDLINE(R)

17650222 PMID: 15784555

A deficiency in gamma interferon or interleukin-10 modulates T-Cell-dependent responses to heat shock protein 60 from Histoplasma capsulatum.

Scheckelhoff Mark; Deepe George S

Department of Molecular Genetics, Biochemistry, and Microbiology, University of Cincinnati College of Medicine, Cincinnati, OH 45267-0560, USA.

Infection and immunity (United States) Apr 2005, 73 (4) p2129-34, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI34361; AI; NIAID; AI42747; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Immunization of mice with **heat shock protein** 60 from Histoplasma capsulatum or a polypeptide from the protein designated F3 confers **protection** . Vbeta8.1/8.2+ T cells are critically important for the **protective efficacy** of this antigen. The production of interleukin-10 and gamma interferon following **vaccination** is essential for **efficacy** . In this study, we sought to determine whether the absence of either cytokine modified the repertoire of antigen-reactive T cells and whether it altered the functional properties of T cells. Mice lacking gamma interferon or interleukin-10 manifested a skewed repertoire compared to that of wild-type mice. The bias was most marked in gamma interferon-deficient mice and modestly altered in interleukin-10-deficient animals. The altered repertoire in gamma interferon-deficient mice could not be explained at the level of antigen presentation or by the absence of this population from mice. The proportion of T cells from interleukin-10-deficient mice manifesting a Th1 phenotype was greatly increased compared to that from wild-type animals. Transfer of splenocytes from gamma interferon- or interleukin-10-deficient mice immunized with heat shock protein 60 failed to confer protection in T-cell receptor alpha/beta-/- mice. The transfer of T-cell clones that did not produce both cytokines failed to prolong survival in T-cell receptor alpha/beta-/- mice, whereas the clones with the same features that were derived from wild-type mice did. These results

indicate that the cytokine milieu influences the shape of the T-cell receptor repertoire and support the importance of gamma interferon and interleukin-10 in the **efficacy** of heat shock protein 60.

Tags: Male; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Chaperonin 60--immunology--IM; *Histoplasma--immunology--IM ; *Interferon Type II--physiology--PH; *Interleukin-10--physiology--PH; *T-Lymphocytes--immunology--IM; Animals; Antigen Presentation; Mice; Mice, Inbred C57BL; Receptors, Antigen, T-Cell, alpha-beta--physiology--PH

CAS Registry No.: 0 (Chaperonin 60); 0 (Receptors, Antigen, T-Cell, alpha-beta); 130068-27-8 (Interleukin-10); 82115-62-6 (Interferon Type II)

Record Date Created: 20050323

Record Date Completed: 20050414

25/9/2

DIALOG(R)File 155:MEDLINE(R)

18775308 PMID: 16233848

Screening of cytokines to enhance vaccine effects of heat shock protein 70-rich tumor cell lysate.

Ito Akira; Fujioka Masatake; Tanaka Kouji; Kobayashi Takeshi; Honda Hiroyuki

Department of Biotechnology, School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan.

J Biosci Bioeng (Japan) Jul 2005, 100 (1) p36-42, ISSN 1389-1723 Journal Code: 100888800

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Subfile: INDEX MEDICUS

Heat shock proteins (**HSPs**) have been recognized as significant participants in immune reactions. We have previously reported that heat-treated cells expressing **HSP70** can mediate potent antitumor immune responses. As successful immunotherapy is dependent on the host immune system, the present study evaluated whether systemic administration of immunocyte stimulatory and growth promoting cytokines could enhance heat-treated cell lysate **vaccine** (HCLV) immunization to further promote the antitumor immunity. After heating mouse melanoma B16 cells (43 degrees C, 30 min) to elicit increased 1HSP70 expression, cells were lysed by freeze thawing to prepare HCLV. In approaches using a poorly immunogenic melanoma B16, the effects of various cytokines (IL-1beta, -2, -4, -6 and -12, IFN-beta and -gamma, GM-CSF and TNF-alpha) were assessed in combination with HCLV. Syngenic C57BL/6 mice were immunized subcutaneously with HCLV twice, on days -14 and -7, while cytokines were injected intraperitoneally on day -7. Subcutaneous B16 cell challenge was performed on day 0. IL-12 significantly enhanced the **efficacy** of HCLV, compared to non-heated cell lysate **vaccine** (CLV) and non- **vaccination** . Systemic administration of recombinant IL-12 augmented the **efficacy** of HCLV, inducing **protective** immunity against tumor challenge and enhancing cytotoxicity assessed in primed splenocytes against B16 cells in treated mice. These results suggest that IL-12 represents an important modulator of antitumor immune responses induced by HCLV, and may facilitate further efforts to develop novel cancer immunotherapies based on **HSP70** -mediated **vaccination** .

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L2: Entry 22 of 22 File: DWPI Nov 19, 2002

DERWENT-ACC-NO: 2003-298137
DERWENT-WEEK: 200553

TITLE: Producing antibodies specific for fusion proteins comprising stress proteins e.g. heat shock proteins and heterologous proteins e.g. viral antigen, by inducing immune response in host using fusion protein and collecting antibody

INVENTOR: YOUNG, R A

PATENT-ASSIGNEE: WHITEHEAD INST BIOMEDICAL RES (WHED)

PRIORITY-DATA: 1994US-0336251 (November 3, 1994), 1988US-0207298 (June 15, 1988), 1989US-0366581 (June 15, 1989), 1989WO-US02619 (June 15, 1989), 1991US-0804632 (December 9, 1991), 1993US-0073381 (June 4, 1993), 1994WO-US06362 (June 6, 1994), 1995US-0461720 (June 5, 1995), 1999US-0468041 (December 21, 1999)

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PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6482614 B1	November 19, 2002		029	C12P021/04

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
US 6482614B1	June 15, 1988	1988US-0207298	CIP of
US 6482614B1	June 15, 1989	1989US-0366581	Cont of
US 6482614B1	June 15, 1989	1989WO-US02619	CIP of
US 6482614B1	December 9, 1991	1991US-0804632	CIP of
US 6482614B1	June 4, 1993	1993US-0073381	CIP of
US 6482614B1	June 6, 1994	1994WO-US06362	CIP of
US 6482614B1	November 3, 1994	1994US-0336251	Cont of
US 6482614B1	June 5, 1995	1995US-0461720	Cont of
US 6482614B1	December 21, 1999	1999US-0468041	
US 6482614B1		US 6338952	Cont of

INT-CL (IPC): C12 N 5/06; C12 P 21/04; G01 N 33/53

RELATED-ACC-NO: 1990-022380;1995-036486 ;2002-163203 ;2002-215020 ;2003-625518 ;2005-521375

ABSTRACTED-PUB-NO: US 6482614B
BASIC-ABSTRACT:

NOVELTY - Obtaining purified antibodies that specifically bind a fusion protein which comprises a stress protein or its portion, and a heterologous protein or peptide, involves introducing a fusion protein into a mammalian host, to induce an immune response, removing a sample comprising antibodies from the host, and purifying antibodies that specifically bind the fusion protein from the sample.

USE - The method is useful for obtaining purified antibodies that specifically bind a fusion protein comprising a stress protein or its portion, and a heterologous protein or peptide. The stress protein is a heat shock protein, preferably hsp90, hsp70 or hsp60. The stress protein is a member of the small molecular weight hsp family, preferably a member of groES or Dnaj family, or a human, murine, rat, fungal, parasite or bacterial stress protein. The bacterial stress protein is a member of DnaJ, DnaK, GroES or GroEL stress protein family. The stress protein is a mycobacterial stress protein, preferably a Mycobacterium tuberculosis (71, 65 or 12 kDa protein), M. leprae (70, 65 or 18 kDa protein) or M. bovis Bacille Calmette Guerin (BCG) stress protein (hsp60). The heterologous protein or peptide is a cancer cell-associated antigen, such as GD3, GM2, Gb3, Forssman antigen, Sialosyl-Lea, melanoma antigen, carcino-embryonic antigen (CEA), alpha -fetoprotein, prostate specific antigen, or a Tn antigen, a viral antigen such as human immunodeficiency virus (HIV) antigen e.g. HIV gag or pol protein or peptide, an influenza virus antigen such as hemagglutinin, or a parasitic antigen (claimed).

ABSTRACTED-PUB-NO: US 6482614B
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/7

DERWENT-CLASS: B04 D16
CPI-CODES: B04-B04C; B04-G01; B04-N08; B11-C07A; D05-H07; D05-H11;

Previous Doc Next Doc Go to Doc#

L2: Entry 5 of 22 File: PGPB Oct 31, 2002

DOCUMENT-IDENTIFIER: US 20020161192 A1
TITLE: Helicobacter pylori live vaccine

Summary of Invention Paragraph:
[0032] Further, the immunogens HylB, citrate synthase, GroEL and GroES can be used for the manufacture of a broad range live vaccine against microbial infections. This is due to their high homology between different microbial species which leads to cross protection from infections with one or several pathogenic microbial species (see e.g. FIG. 9 or 10). Thus, in addition to the respective immunogens from Helicobacter, the immunogens may be derived from other microbial species. The homology on the amino acid level (i.e. the percentage of identical amino acids) to the respective Helicobacter proteins may be at least 30%, 40%, 50%, 60%, 70%, 80%, 90% or even 95%, in increasing order of preference.

Summary of Invention Paragraph:
[0033] The nucleic acid sequence coding for said immunogens HylB, citrate synthase, GroEL or GroES can be derived from a bacterium such as Helicobacter spec., Shigella spec., Neisseria spec., Staphylococcus spec., Streptococcus spec., Pneumococcus spec., Pseudomonas spec., Treponema spec., Chlamydia spec., Mycobacterium spec., Bordetella spec., Clostridium spec., Salmonella spec., Campylobacter spec., Francisella spec., Coxiella spec., Haemophilus spec., Enterococcus spec., Enterobacter spec., Pasteurella spec., Vibrio spec., Klebsiella spec., Bartonella spec., Escherichia spec., Serratia spec., Bacillus spec., Legionella spec., Erwinia spec., Rickettsia spec., or Yersinia spec. However, microbial organisms other than bacteria such as Leishmania spec., Plasmodium spec., Trypanosoma spec or Amoeba spec. might be suitable as well.

Summary of Invention Paragraph:
[0034] Instead of whole proteins also portions thereof such as immunogenic fragments, epitopes or clusters of epitopes can be used for the manufacture of said live vaccine. A selected T-cell epitope which is suitable for obtaining cross protection between Helicobacter and Yersinia is depicted in FIG. 8. T-cell epitopes typically comprise 8-15 amino acids in length but may vary in a length range from at least 5 amino acids to about maximally 20 amino acids. Further T-cell epitopes can be predicted from databases using i.e. the SYFPEITHI algorithm (Rammnensee, H., J. Bachmann, N. P. Emmerich, O. A. Barhor, and S. Stevanovic. 1999. SYFPEITHI: database for MHC ligands and peptide motifs. Immunogenetics. 50(3-4):213-9), (http://www.uni-tuebingen.de/uni/kxi/). Furthermore, surface exposure and protein hydrophilicity as means of predicting antigenicity, and thus B-cell epitopes may be characterized using algorithms as described by Hopp and Woods (Hopp, T. P., and K. R. Woods. 1983. A computer program for predicting protein antigenic determinants. Mol Immunol. 20(4):483-9) or by Janin and Wodak (Janin, J., and S. Wodak. 1987. Conformation of amino acid side-chains in proteins. J Mol Biol. 125(3):357-86). Thus, epitopes preferably have a maximal length of 30, 20, 15, 10 or even only 5 amino acids and even more preferably between 5 and 20 and most preferably between 8 and 15 amino acids. Preferably, the use of overlapping epitopes between human and microbial immunogens such as GroEL or GroES is avoided

Summary of Invention Paragraph:
[0036] Recombinant GroES and GroEL proteins (corresponding with HP0010 and HP0011)

from Helicobacter pylori were successfully employed in a prophylactic vaccination approach in mice using purified proteins as subunit vaccines as described by Ferrero et al. 1995 (Ferrero, R. L., J. M. Thiberge, I. Kansau, N. Wuscher, M S Huerre, and A. Labigne. 1995. The GroES homolog of Helicobacter pylori confers protective immunity against mucosal infection in mice. Proc Natl Acad Sci USA. 92 (14):6499-503).

Summary of Invention Paragraph:
[0043] A preferred embodiment of an in vivo inducible expression system relates to the use of expression signals from the groES/EL operon. It is known (Buchmeier, N. A., and F. Heffron. 1990. Induction of Salmonella stress proteins upon infection of macrophages. Science. 248(4956):730-2) that expression of groES/EL in Salmonella is up-regulated as a consequence of interaction with the host, possibly due to the host's oxidative burst and other immunological events or fever. The operon structure of Salmonella typhimurium groES/EL is depicted in FIG. 11, (drawn from GenBank AS033231). Expression signals from the groELES operon comprise the promoter, a 5' untranslated region, ribosome binding sites and/or the intergenic region between groES and groEL. Instead of or additionally to either groES or groEL gene sequence, any other nucleic acid, preferentially coding for an immunogen, can be introduced in said operon structure. This is accomplished by in-frame insertions, out-of-frame insertions, partial or complete substitution of groES or groEL and/or 3' terminal appending of the nucleic acid coding for immunogens as described above. Thus, a further aspect of the invention relates to an expression system in a host cell for the expression of a nucleic acid molecule coding for an immunogen or fragment or epitope thereof heterologous to said host cell, comprising homologous or heterologous expression signals from the groES/EL operon and optionally a nucleic acid molecule coding for a GroES and/or GroEL protein.

Summary of Invention Paragraph:
[0047] The expression product of the nucleic acid molecule coding for an immunogen, particularly a HylB, a citrate synthase, GroEL or GroES protein may remain in the cytosol of said carrier, may be directed to the inner membrane, to the periplasm or outer membrane of said carrier, or may be secreted. In a more preferred embodiment the expression product is secreted by the type III or by the autotransporter system. Type III secretion is disclosed e.g. in WO98/53854 and an autotransporter system in WO97135022 which are herein incorporated by reference.

Summary of Invention Paragraph:
[0048] The nucleic acid molecule encoding a HylB, citrate synthase, GroEL or GroES protein or an immunogenic fragment or an epitope thereof can be homologous or heterologous to the employed carrier. For example, the nucleic acid molecule may be derived from an organism different from the carrier or the nucleic acid molecule may be derived from the carrier organism and being overexpressed in the carrier.

Summary of Invention Paragraph:
[0049] The immunogens can be expressed as single proteins or as proteins fused to an other immunogenic protein or fragment thereof wherein the immunogens can be either homologous or heterologous to the carrier as discussed above. In an even further preferred embodiment a nucleic acid molecule encoding a heterologous HylB, citrate synthase, GroEL or GroES protein or a fragment thereof is expressed as a fusion protein with a HylB, citrate synthase, GroEL or GroES protein homologous to the employed carrier organism or a fragment thereof, wherein a fusion protein containing heterologous and homologous portions is obtained.

Summary of Invention Paragraph:
[0050] In order to obtain a multivalent immunogen, several different immunogenic proteins can be expressed in the bacterial carrier. Thus, the invention also relates to a bacterial carrier capable of presenting a plurality of immunogens, particularly selected from HylB, citrate synthase, GroEL and GroES and optionally at least one further immunogen which is encoded by at least one further

heterologous nucleic acid molecule. More preferably, the plurality of immunogens is selected from at least two proteins having immunogenic properties that induce at least partial protection against bacterial, viral or parasitic infection such as HylB, citrate synthase, GroES, GroEL (used in combination with each other), UreA, UreB, or catalase of H. pylori, listeriolysin and p60 of Listeria monocytogenes CFAI or CFAII of enterotoxigenic E. coli, F1 antigen of Yersinia pestis and others.

Summary of Invention Paragraph:
[0052] Thus, in an even more preferred embodiment, the multivalent immunogen is encoded by a nucleic acid molecule encoding a HylB, citrate synthase, GroES or GroEL protein or a fragment or an epitope thereof operatively linked to a further nucleic acid molecule encoding a further immunogen yielding a hybrid nucleic acid molecule encoding a fusion protein having at least two determinants. It should be noted that genetic fusions of three or more immunogenic components are also suitable.

Summary of Invention Paragraph:
[0054] As described above, the use of said nucleic acid molecules for the manufacture of a live vaccine comprises the preparation of a bacterial carrier expressing one or more microbial immunogens. Thus, a further aspect relates to a recombinant carrier cell, which comprises at least one nucleic acid molecule encoding a HylB, a citrate synthase, a GroEL or a GroES protein or an immunologically active fragment or an epitope thereof, wherein said cell is capable of expressing said nucleic acid molecule and inducing protective immunity against a microbial infection in a mammalian host. The immunity may be induced against the carrier bacterium and a single pathogen from which the immunogen is derived such as Helicobacter but might also confer a broad range immunity against several microbial pathogens due to cross protection. In a preferred embodiment the bacterial carrier is an attenuated Salmonella cell.

Summary of Invention Paragraph:
[0058] In a further embodiment, at least one further heterologous nucleic acid molecule can be expressed encoding an immunogen or a fragment or an epitope thereof. This fusion protein can comprise a HylB, citrate synthase, GroES or GroEL protein or a fragment or an epitope thereof with the expression product of the further nucleic acid molecule.

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L2: Entry 15 of 22 File: USPT Jul 10, 2001

DOCUMENT-IDENTIFIER: US 6258359 B1
** See image for Certificate of Correction **
TITLE: Immunogenic compositions against helicobacter infection, polypeptides for use in the compositions, and nucleic acid sequences encoding said polypeptides

Detailed Description Text (241):
In common with other organisms, H. pylori bacteria express heat-shock proteins (SEQ ID NO: 29-30) that share homologies with the GroES and GroEL class of proteins from Escherichia coli. We have assessed the heat-shock proteins of H. pylori as potential protective antigens in a murine model of gastric Helicobacter infection. Orogastric immunization of mice with recombinant H. pylori GroES- and GroEL-like proteins protected 80S (n=20) and 70% (n=10) of animals, respectively, from a challenge dose of 10.sup.4 Helicobacter bacteria (versus control mice: P=0.0042 and P=0.0904, respectively). All mice (n=19) that were immunized with a dual antigen preparation, consisting of H. pylori GroES-like protein and the B subunit of H. pylori urease (SEQ ID NO: 26), were protected against infection. This represented an equivalent level of protection as that provided by a sonicated Helicobacter extract (P=0.955) Antibodies directed against the recombinant H. pylori antigens were predominantly of the IgG.sub.1 class, suggesting a type 2 T-helper cell (Th-2) response was involved in protection.

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L2: Entry 16 of 22 File: USPT Jun 19, 2001

DOCUMENT-IDENTIFIER: US 6248330 B1
** See image for Certificate of Correction **
TITLE: Immunogenic compositions against helicobacter infection, polypeptides for use in the compositions, and nucleic acid sequences encoding said polypeptides

Detailed Description Text (235):
In common with other organisms, H. pylori bacteria express heat-shock proteins (SEQ ID NOS:29-30) that share homologies with the GroES and GroEL class of proteins from Escherichia coli. We have assessed the heat-shock proteins of H. pylori as potential protective antigens in a murine model of gastric Helicobacter infection. Orogastric immunization of mice with recombinant H. pylori GroES- and GroEL-like proteins protected 80% (n=20) and 70% (n=10) of animals, respectively, from a challenge dose of 10.sup.4 Helicobacter bacteria (versus control mice: P=0.0042 and P=0.0904, respectively). All mice (n=19) that were immunized with a dual antigen preparation, consisting of H. pylori GroES-like protein and the B subunit of H. pylori urease (SEQ ID NO:26), were protected against infection. This represented an equivalent level of protection as that provided by a sonicated Helicobacter extract (P=0.955). Antibodies directed against the recombinant H. pylori antigens were predominantly of the IgG.sub.1 class, suggesting a type 2 T-helper cell (Th-2) response was involved in protection.

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L2: Entry 21 of 22 File: USPT Dec 10, 1991

DOCUMENT-IDENTIFIER: US 5071962 A
TITLE: Nucleotide, deduced amino acid sequence, isolation and purification of heat-shock chlamydial proteins

Detailed Description Text (3):
The invention also relates the HypB chlamydial bacterial protein encoded in the hyp B gene, which is characterized as follows: (a) it is endogenous to and extractable from chlamydial elementary bodies (EBs) and reticulate bodies (RBs), (b) it produces delayed ocular and dermal inflammatory responses in mammals, (c) it is reactive with antiserum produced by antigens extracted from chlamydial EBs, (d) it can be purified essentially free of other material by standard biochemical and immunological techniques, (e) it has a molecular weight in SDS PAGE gels of about 57,000 D, (f) it is highly soluble, (h) it is very immunogenic, (i) it contains chlamydial specific epitopes, and (j) it contains epitopes common to other ca. 60kD stress-response proteins. In one embodiment, the protein of the invention has the amino acid sequence set forth in FIG. 5. In another embodiment, the HypB protein of the present invention has the amino acid sequence as set forth in FIG. 7. Indeed, the chlamydial HypA and HypB proteins are homologues of the E. coli GroES and GroEL heat shock proteins (HSP), respectively; and the HypB protein is a member of a widely conserved family of prokaryotic and eukaryotic stress response proteins referred to as HSP60.The invention also relates to unique portions of the HypB chlamydial bacterial protein described above, for example, a unique portion (at least 5 or 6 amino acids) of the sequence set forth in FIG. 5 or FIG. 7. The HypB protein substantially free of proteins with which it is normally associated can be bound to a solid support such as, for example, agarose, sepharose, plastic, nylon membrane or nitrocellulose paper.

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